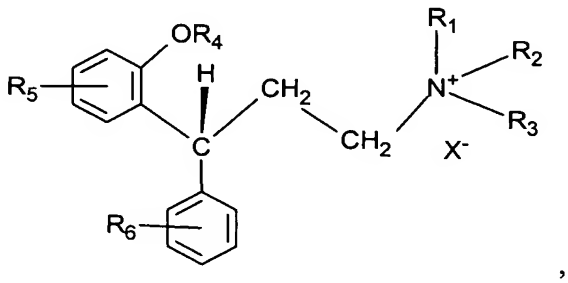
We Claim:

1. A method of treating chronic obstructive pulmonary disease (COPD) in a mammal, comprising administering a first pharmaceutical agent and a second pharmaceutical agent, wherein the first pharmaceutical agent comprises a compound of formula I



I

or an enantiomer thereof, wherein:

each R_1, R_2, and R_3 is independently H, C_1-C_5 alkyl optionally substituted with phenyl, or C_2-C_6 alkenyl; or

two of R_1, R_2 and R_3 may form a ring together with the quaternary ammonium nitrogen;

R_4 is

–H,

-CO-R_{4-1}, where R_{4-1} is

C_1-C_4 alkyl,

C_1-C_4 alkoxy, or

-$NR_{4-2}R_{4-3}$, where R_{4-2} and R_{4-3} are the same or different and are –H or C_1-C_4 alkyl;

R_5 and R_6 are the same or different and are

-H;

C_1-C_4 alkyl optionally substituted with 1 or 2

-OH,

C_1-C_4 alkoxy,

-COOH, or

-CO-O-(C_1-C_3 alkoxy);

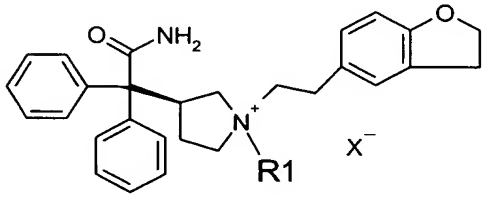
-F, -Cl, or Br; or

-CF_3;

where X^- is an anion of hydrochloric acid; hydrobromic acid; hydroiodic acid; sulfuric acid; phosphoric acid; nitric acid; citric acid; methanesulfonic acid; CH_3-$(CH_2)_n$-COOH where n is 0 to 4; HOOC-$(CH_2)_m$-COOH, where m is 1 to 4; HOOC-CH=CH-COOH; or benzoic acid; and

the second pharmaceutical agent is an Adenosine A_{2a} Receptor Agonist, a D2-Dopamine Receptor Agonist, a PDE Inhibitor, a corticosteroid, a norepinephrine reuptake inhibitor, or 4-hydroxy-7-[2-[2-[3- [2-phenylethoxy]-propylsulphonyllethylamino] ethyl] -1,3-benzothiazol-2(3H)-one.

2. A method of treating chronic obstructive pulmonary disease (COPD) in a mammal, which method comprises administering a first pharmaceutical agent and a second pharmaceutical agent, wherein the first pharmaceutical agent is a compound of formula II



II

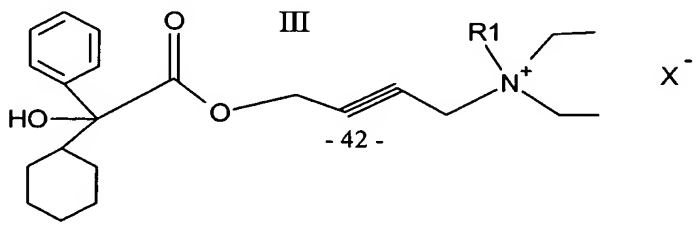
or a stereoisomer thereof, wherein

R_1 is C_1-C_6 alkyl, -CH_2-(C_1-C_4 alkenyl), or –CH_2-(C_1-C_6 alkynyl), each of which is optionally substituted with phenyl, C_1-C_4 alkoxy, or hydroxyl; and

X^- is an anion of a pharmaceutically acceptable acid; and

the second pharmaceutical agent is an Adenosine A_{2a} Receptor Agonist, a D2-Dopamine Receptor Agonist, a PDE Inhibitor, a corticosteroid, a norepinephrine reuptake inhibitor, or 4-hydroxy-7-[2-[2-[3- [2-phenylethoxy]-propylsulphonyllethylamino] ethyl] -1,3-benzothiazol-2(3H)-one.

3. A method of treating chronic obstructive pulmonary disease (COPD) in a mammal, which method comprises administering a first pharmaceutical agent and a second pharmaceutical agent, wherein the first pharmaceutical agent is a compound of formula III



III

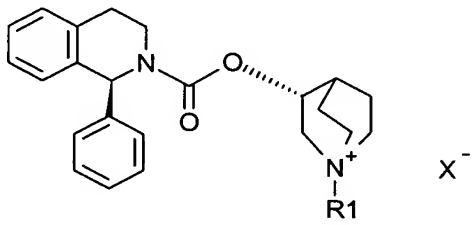
or a stereoisomer thereof, wherein

R_1 is C_1-C_6 alkyl, -CH_2-(C_1-C_4 alkenyl), or –CH_2-(C_1-C_6 alkynyl), each of which is optionally substituted with phenyl, C_1-C_4 alkoxy, or hydroxyl; and

X^- is an anion of a pharmaceutically acceptable acid,; and

the second pharmaceutical agent is an Adenosine A_{2a} Receptor Agonist, a D2-Dopamine Receptor Agonist, a PDE Inhibitor, a corticosteroid, a norepinephrine reuptake inhibitor, or 4-hydroxy-7-[2-[2-[3- [2-phenylethoxy]-propylsulphonyllethylamino] ethyl] -1,3-benzothiazol-2(3H)-one.

4. A method of treating chronic obstructive pulmonary disease (COPD) in a mammal, which method comprises administering a first pharmaceutical agent and a second pharmaceutical agent, wherein the first pharmaceutical agent is a compound of formula IV



IV

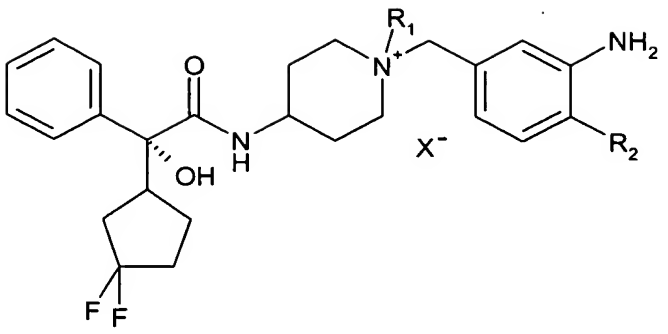
or a stereoisomer thereof, wherein

R_1 is C_1-C_6 alkyl, -CH_2-(C_1-C_4 alkenyl), or –CH_2-(C_1-C_6 alkynyl), each of which is optionally substituted with phenyl, C_1-C_4 alkoxy, or hydroxyl; and

X^- is an anion of a pharmaceutically acceptable acid; and

the second pharmaceutical agent is an Adenosine A_{2a} Receptor Agonist, a D2-Dopamine Receptor Agonist, a PDE Inhibitor, a corticosteroid, a norepinephrine reuptake inhibitor, or 4-hydroxy-7-[2-[2-[3- [2-phenylethoxy]-propylsulphonyllethylamino] ethyl] -1,3-benzothiazol-2(3H)-one.

5. A method of treating chronic obstructive pulmonary disease (COPD) in a mammal, which method comprises administering a first pharmaceutical agent and a second pharmaceutical agent, wherein the first pharmaceutical agent is a compound of formula V



V

or a stereoisomer thereof, wherein

R_1 is C_1-C_6 alkyl, -CH_2-(C_1-C_4 alkenyl), or –CH_2-(C_1-C_6 alkynyl), each of which is optionally substituted with phenyl, C_1-C_4 alkoxy, or hydroxyl;

R_2 is H or OH; and

X^- is an anion of a pharmaceutically acceptable acid; and

the second pharmaceutical agent is an Adenosine A_{2a} Receptor Agonist, a D2-Dopamine Receptor Agonist, a PDE Inhibitor, a corticosteroid, a norepinephrine reuptake inhibitor, or 4-hydroxy-7-[2-[2-[3- [2-phenylethoxy]-propylsulphonyllethylamino] ethyl] -1,3-benzothiazol-2(3H)-one.

6. The method of claim 2, 3, 4 or 5 wherein X^- is an anion of tartaric acid; hydrochloric acid; hydrobromic acid; hydroiodic acid; sulfuric acid; phosphoric acid; nitric acid; citric acid; methanesulfonic acid; CH_3-(CH_2)$_n$-COOH, where n is 0 to 4; HOOC-(CH_2)m-COOH, where m is 1 to 4; HOOC-CH=CH-COOH; or benzoic acid.

7. The method of claim 1, 2, 3, 4 or 5 wherein X^- is iodide, bromide, or chloride.

8. The method of claim 1, 2, 3, 4 or 5 comprising administering a pharmaceutical composition of a compound of the formula I, II, III, IV or V.

9. The method of claim 8 wherein the pharmaceutical composition comprises between about 1 mg and about 1000 mg of the compound of the formula I, II, III, IV or V.

10. The method of claim 9 wherein the pharmaceutical composition comprises between about 200 mg and about 800 mg of the compound of the formula I, II, III, IV or V.

11. The method of claim 9 wherein the pharmaceutical composition comprises about 600 mg of the compound of the formula I, II, III, IV or V.

12. The method of claim 1,2, 3, 4 or 5 wherein the compound of the formula I, II, III, IV or V is administered via inhalation or insufflation.

13. A method of treating chronic obstructive pulmonary disease (COPD) in a mammal, comprising administering a first pharmaceutical agent and a second pharmaceutical agent, wherein the first pharmaceutical agent is
(3R)-3-(2-hydroxy-5-methylphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium iodide;
(3R)-3-(2-hydroxy-5-methylphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium bromide;
(3R)-N-ethyl-3-(2-hydroxy-5-methylphenyl)-N,N-diisopropyl-3-phenylpropan-1-aminium iodide;
(3R)-3-(2-hydroxy-5-methylphenyl)-N,N-diisopropyl-3-phenyl-N-propylpropan-1-aminium iodide;
(3R)-N-benzyl-3-(2-hydroxy-5-methylphenyl)-N,N-diisopropyl-3-phenylpropan-1-aminium iodide;
(3R)-N-(tert-butyl)-3-(2-hydroxy-5-methylphenyl)-N,N-dimethyl-3-phenylpropan-1-aminium bromide;
(3R)-3-[2-hydroxy-5-(hydroxymethyl)phenyl]-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium iodide;
(3R)-3-(2-hydroxyphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium bromide;
(3S)-3-(2-hydroxyphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium bromide;
(3R)-3-(5-chloro-2-hydroxyphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium bromide;

(3R)-3-(5-bromo-2-hydroxyphenyl)-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium bromide;

(3R)-3-[2-(acetyloxy)-5-methylphenyl]-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium iodide;

(3R)-3-[2-(isobutyryloxy)-5-methylphenyl]-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium iodide;

(3R)-3-(4-fluorophenyl)-3-(2-hydroxy-5-methylphenyl)-N,N-diisopropyl-N-methylpropan-1-aminium bromide;

(3R)-3-[2-hydroxy-5-(trifluoromethyl)phenyl]-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium bromide;

(3R)-3-[2-(isobutyryloxy)-5-hydroxymethylphenyl]-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminium bromide;

(3R)-3-{2-(acetyloxy)-5-[(acetyloxy)methyl]phenyl}-N,N-diisopropyl-N-methyl-3-phenylpropan-1-aminiumbromide;

2-{(1R)-3-[diisopropyl(methyl)ammonio]-1-phenylpropyl}-4-methylbenzenolate;

1-[3-(2-hydroxy-5-methylphenyl)-3-phenylpropyl]-1-(2-methylprop-2-enyl)pyrrolidinium bromide;

1-[3-(2-hydroxy-5-methylphenyl)-3-phenylpropyl]-1-(3-methylbut-2-enyl)pyrrolidinium bromide;

1-allyl-1-[3-(2-hydroxy-5-methylphenyl)-3-phenylpropyl] pyrrolidinium iodide;

1-allyl-1-[3-(2-hydroxy-5-methylphenyl)-3-phenylpropyl] pyrrolidinium chloride;

3-(2-hydroxy-5-methylphenyl)-N,N-diallyl-N-methyl-3-phenyl propan-1-aminium iodide;

3-(2-hydroxy-5-methylphenyl)-N,N-diallyl-N-ethyl-3-phenylpropan-1-aminium iodide;

1-allyl-1-[3-(2-hydroxy-5-methylphenyl)-3-phenyl propyl]piperidinium chloride;

3-(2-hydroxy-5-methylphenyl)-N,N,N-triallyl-3-phenylpropan-1-aminium bromide;

(3S)-3-(2-amino-2-oxo-1,1-diphenylethyl)-1-[2-(2,3-dihydro-1-benzofuran-5-yl)ethyl]-1-methylpyrrolidinium iodide;

4-(diethylmethylaminium)-2-butynyl alpha phenyl cyclohexane glycolate iodide;

3-methyl-3-quinuclindinyl 1-phenyl-2-isoindolinecarboxylate; or

(2R)-N-[1-(6-aminopyridin-2-ylmethyl)1-methylpiperdin-4-yl]-2-[(1R)-3,3,-difluorocyclopentyl]-2-hydroxy-2-phenylacetamide iodide; and

the second pharmaceutical agent is an Adenosine A_{2a} Receptor Agonist, a D2-Dopamine Receptor Agonist, a PDE Inhibitor, a corticosteroid, a norepinephrine reuptake inhibitor, or 4-hydroxy-7-[2-[2-[3- [2-phenylethoxy]-propylsulphonyllethylamino] ethyl] -1,3-benzothiazol-2(3H)-one.

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